### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

 In re application of:
 Cantor et al.
 Confirmation No.:
 6905

 Application No.:
 10/655,762
 Group No.:
 1637

 Filed:
 September 5, 2003
 Examiner: KIM, YOUNG J

For: QUANTIFICATION OF GENE EXPRESSION

#### DECLARATION OF DR. CHARLES CANTOR

- I, Charles Cantor, Ph.D., declare as follows:
- I am a co-inventor in the above-identified patent application.
- 2. I have served as chair and professor of the department of biomedical engineering and biophysics, and Director of the Center for Advanced Biotechnology at Boston University since 1992. Prior to that time, I held positions at Columbia University and the University of California, Berkeley. I have also been the Director of the Human Genome Center Project of the Department of Energy at Lawrence Berkeley Laboratory. In 1998, I joined Sequenom, Inc. as a Chief Scientific Officer and Chairman of the Scientific Advisory Board. In May 2000, I was appointed to the Company's board of directors. I am a consultant to more than 16 biotech firms, and I have published more than 400 peer reviewed articles. I have been granted over 50 US patents, and I have co-authored a three-volume textbook on Biophysical Chemistry. I published the first textbook on genomics entitled, Genomics: The Science and Technology of the Human Genome Project. Accordingly, I have significant experience and expertise in use and development of methods used for nucleic acid analysis, including nucleic acid quantification.
- 3. A true copy of my current curriculum vitae is attached herewith.
- 4. I have been advised that the Examiner has cited the following three articles in connection with the examination of the above-identified patent application: Becker-André and Hahlbrock, Nucleic Acid Research 17 (22): 9437-9446, 1998 ("Becker"), Amexis et al., Proc. Natl. Acad. Sci. U.S.A. 98 (21): 12097-12102, 2001 ("Amexis") and Ross et al, Biotechniques, 29 (3): 620-629, 2000 ("Ross").

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- 5. I have been advised also that the Examiner has argued that "The absolute quantitation is based on the comparing the amount of signal determined from the target nucleic acid against the amount of signal determined from known varying amounts of standard nucleic acids (i.e., standard curve) [Becker] and since the MALDL-TOF assay produced consistent and reliable quantitation of signals, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success at combining the teachings of the references, thereby arriving at the invention as claimed." See May 11, 2009 Office Action, page 9, paragraph 2 of; emphasis added.
- I disagree with the Examiner's assertions for the reasons explained in detail below.
- Becker quantified a nucleic acid using a standard that differed by one nucleotide from the target so that a restriction enzyme would digest one of the amplified nucleic acids.
- 8. Although Becker discussed the possibility of absolute quantification, Becker required an extra step of diluting the PCR reaction mixture prior to the last PCR cycle in the amplification step in order to be quantitative and determine an absolute amount of the target nucleic acid.
- 9. Becker especially emphasized the importance of this diluting step for the purpose of comparing the amount of signal determined from the target nucleic acid against the amount of signal determined from the standard nucleic acids, as cited:

"Using a mixture of authentic (endogenous = en) and mutated (exogenous = ex) in vitro RNA<sup>4Cl</sup> transcripts we could show that the ratio of signal intensities of the detected bands represented the ratio of RNA amounts present in the beginning. However, it was crucial to dilute the sample before the last PCR cycle. Otherwise, the upper band (en) was consistently over-represented." See Becker, page 9440, paragraph 2, lines 1-6; emphasis added.

Moreover, Becker also described that this dilution step is necessary for absolute quantification of nucleic acid in order to avoid the problem of "heterodimeric DNA" phenomenon after certain cycle numbers of PCR amplification. See Becker, e.g., page 9440, paragraph 2, lines 7-12; page 9443, paragraph 2, lines 1-5. Therefore, without the dilution step, the result of quantification in Becker would not have been accurate, and the quantification of an absolute amount of target would have been greatly compromised.

10. In contrast, we have explicitly addressed in the specification that the absolute quantification method of the claimed invention needs virtually no optimization for PCR Application No. 10/655,762 Declaration of Dr. Charles Cantor Page 3 of 6

amplification. Hence we do not need the dilution step in any of the PCR cycles. Our absolute quantification method is also independent of PCR cycle numbers.

- 11. Also, the heterodimeric DNA problem means that the accuracy of each assay will be different and accounting for this difference requires a correction factor that will be different for each assay (every target). Our method does not have to make adjustments specific to each target. Therefore, for the reasons provided above, Becker does not teach or suggest a method that would be useful as an absolute quantification method and/or allow at least two or more targets to be analyzed simultaneously.
- 12. It is my opinion, that if it had been obvious to use Becker to design an absolute quantification method using mass spectrometry, which has been generally known as an analysis tool since at least the mid 1980's with commercial instruments introduced in the early 1990s, it would not have taken over 10 years from the publication of Becker to develop such a method.
- Neither Amexis nor Ross even mention that their methods can be applied for absolute quantification.
- 14. I am intimately aware of what is described in Amexis as I am one of the co-authors of the article. Amexis quantified the relative levels of two virus variants in one reaction through PCR and MassArray system. See Amexis, e.g., page 12100, first column, last paragraph. Comparing the relative amount of allelic variants does not allow absolute quantification of nucleic acid species in the reaction. Additionally, because Amexis evaluated relative amounts of allelic products already in the sample, Amexis did not add an external standard.
- 15. Ross also quantified the relative levels of pooled allelic variants and therefore, for the same reason as Amexis, does not describe how absolute quantification could be achieved. See Ross, e.g., page 624, first column, paragraphs 1 and 2. Also Ross did not use an external standard.
- 16. Both Amexis and Ross compared the relative amount of allelic variants; therefore, targets analyzed by the methods described by Amexis and Ross are limited to those targets that comprise an allele (e.g., polymorphism). In contrast, the methods we describe are polymorphism-independent, thus allowing for the absolute quantification of a wider range of targets (e.g., gene sequences that do not contain a polymorphism).

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- 17. It is well known and also stated in Ross that single base extension, like the one used in the presently claimed methods, produces mass differences between 9 and 40 Da.
- 18. However, Ross specifically states that "baseline resolution between alleles differing by 16 Daltons (Da) or less may not be observed" (p. 622, 1st col.).
- 19. Ross also states that "area measurement of a low-intensity extension produces within 40 Da of another allele may be confounded by trace cation...adducts onto the lower mass allele" (p. 622, 1st col.).
- 20. Therefore, Ross teaches that they made sure that all primer extensions resulted in mass differences between 300-400 Da. Page 622, 1st col.). Ross specifically taught that "two related strategies were selected by which a molecular weight separation of about 300-400 Da between allele products of a given locus could be achieved during the primer extension assay." See Ross, page 622, paragraph 3, lines 1-6. Ross expected a clear separation of 300-400 Da between alleles and extension products for reliable peak detection and reliable quantification of nucleic acids. One strategy of Ross terminated the variants of the nucleic acid by one (wild-type) and two (mutant) bases, thus enhanced the mass difference; and the other strategy terminated the variants of the nucleic acid by one base (wild-type) and a fluorescently labeled base (mutant). Neither one of the modified primer extension strategies of Ross, is the same as the single-base primer extension method of the present invention.
- Single base extension like the one we used, does not produce mass differences of 300-400 Da.
- 22. Therefore, Ross teaches against or away from the method we found to be most effective for absolute quantification purposes.
- 23. In view of the above, it is my opinion that one of ordinary skill in the art would not have expected that combination of the mutation analysis of Becker with MALDO-TOF analysis using a single base extension could be used to provide accurate quantitative measurements of the absolute amount of nucleic acids in a sample.
- 24. Even if one were to combine the references, one would be expected to use dilution of PCR mixture before last PCR cycle to obtain a sample that might allow absolute quantification and one would have not used a single base extension but an extension reaction that would have

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resulted in differences between 300-400 Da in molecular weight of the control and the allele one wishes to quantify.

- 25. Moreover, one would have been skeptical about quantifying after the dilution step because it could have been considered to lead to a very low amount of sample that would have lowered the peak intensity, sacrificed the signal to noise level and returned an unreliable quantification result when using MALDI-TOF. Therefore, based on this, it is my opinion that one would not have expected the combination of Becker with Ross and/or Amexis to work.
- 26. In contrast, as already presented in the previous response, we surprisingly discovered that we can accurately quantify the absolute amount of multiple target sequences with multiple internal standards in the same reaction (e.g., triplex targets). We found that the extension products were clearly separated in the mass spectrum with very strong signal to noise level. In particular, the mass differences between several extension products were very small. For example, mass difference between glut3-S and glut3-A was only about 20-25 Da, yet, contrary to what Ross described, we found that the two peaks were clearly separated with strong peak intensities. See September 10, 2007 Response, page 6, last paragraph to page 7, paragraph 2 and Exhibit A. These absolute quantification results by multiplex reactions agreed well with those from uniplex reactions. Moreover, we found that the same method can be used to quantify at least about 20 targets in one multiplex reaction.
- 27. In summary, at the time of the invention, absolute quantification of multiple nucleic acids using mass spectrometric detection and single base extension reactions in the same reaction was not something scientists performed or would have expected to succeed. One skilled in the art would not have been motivated to use internal standards with multiplex target nucleic acids for absolute quantification of multiplex without diluting the amplified mixtures, and one would not have been motivated to subsequently use mass spectrometric analysis combined with single-base primer extension for absolute quantification of multiple nucleic acids in the same reaction, particularly when the multiple nucleic acids differentiating only by small mass differences.

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28. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, and that such willful false statements may jeopardize the validity of the application or any patent that issues therefrom.

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Date	Charles Cantor

# Charles R. Cantor

#### Curriculum Vitae

Born: August 26, 1942; Brooklyn, New York

### Education

1963 A.B., Columbia University, Summa Cum Laude 1966 Ph.D., University of California, Berkeley Eastman Kodak Award

Research Sponsor: Prof. I, Tinoco, Jr.

## Employment

1966-1969 Assistant Professor of Chemistry, Columbia University 1969-1972 Associate Professor of Chemistry, joint appointment in

Biological Sciences, Columbia University

Professor of Chemistry, joint appointment in Biological Sciences, 1972-1981

Columbia University

1981-1989 Professor and Chairman of Genetics and Development,

College of Physicians and Surgeons, Columbia University; and

Deputy Director for Education, 1981-85, Comprehensive Cancer Center; Deputy Director for Biotechnology, 1985-88, Comprehensive Cancer

Center

1988-1989 Higgins Professor of Genetics and Development, Faculty of Medicine,

Columbia University

1988-1990 Director, Human Genome Center, Lawrence Berkeley Laboratory 1989-1991 Senior Biochemist, Cell and Molecular Biology Division, Lawrence

Berkelev Laboratory

Professor of Molecular Biology, University of California, Berkeley 1989-1992 1990-1992 Principal Scientist, Human Genome Project, U.S. Department of Energy 1991-1992 Senior Biochemist, Chemical Biodynamics Division, Lawrence Berkeley

Laboratory

1992-present Professor of Biomedical Engineering and Biophysics, Boston University 1992-present Director, Center for Advanced Biotechnology, Boston University

1994-present Professor, Pharmacology Department, Boston University Medical School 1995-1998 Chair, Department of Biomedical Engineering, Boston University

1998-present Chief Scientific Officer, Sequenom, Inc. and Member, Board of Directors

2001-present Adjunct Professor, Department of Bioengineering, UCSD

### Awards and Honors

1969-1971 Fellow of the Alfred P. Sloan Foundation

1972 Fresenius Award in Chemistry

1973-1974 Guggenheim Fellow

Fairchild Distinguished Visiting Scholar, California Institute of Technology 1975-1976

1978 Eli Lilly Award in Biological Chemistry

Fellow of the American Association for the Advancement of Science 1981

1985 Outstanding Investigator Grant, National Cancer Institute 1988 Biochemical Analysis Prize of the German Society of Clinical Chemistry 1988 Member of the National Academy of Sciences 1988 Member of the American Academy of Arts and Sciences 1989 ISCO Award for Advances in Biochemical Instrumentation 1990 Herbert A. Sober Award, American Society for Biochemistry and Molecular Biology 1990 Honorary Member, Japanese Biochemical Society 1992 Fellow of the California Academy of Sciences 2000 Fellow of the Biophysical Society 2000 Emily M. Gray Award, Biophysical Society 2002 Chief Scientist of the Year, T Sector and BIOCOM 2004 The Ohio State University Human Cancer Genetics Program Commemorative Medal for Excellence in Research and Clinical Care 2006 Fellow of the American Institute for Medical and Biological Engineering Special Lectureships 1985 Distinguished Lecturer, University of Tennessee 1985 Distinguished Lecturer, University of Cincinnati 1985 Jesse Beams Lecturer, University of Virginia 1986 Barton Lecturer, University of Oklahoma 1986 Peter Debve Lecturer, Cornell University Stephanie Lynn Kossoff Memorial Lecturer, Columbia University 1986 1987 Reilly Lecturer, Notre Dame University 1987 Allied Corporation Lecturer, Waksman Institute 1987 Visiting Scholar, Japan Society for the Promotion of Science Veatch Lecturer, Harvard Medical School 1988 1988 Sol Spiegelman Lecturer, University of Illinois 1989 Steinberg/Wylie Lecturer, University of Maryland 1989 Biochemical Society Lecturer, British Association for the Advancement of Science Ronald R. Fisher Lecturer, University of South Carolina 1989 1990 Boyce Thompson Distinguished Lecturer, Cornell University 1990 Distinguished Lecturer, Oak Ridge National Laboratory 1991 Hanna Memorial Lecturer, Case Western Reserve University 1991 Distinguished Speaker in Biochemistry and Molecular Biology, University of Wisconsin, Milwaukee

1997 University Lecturer, Boston University
 1998 Distinguished Lecturer, George Mason University
 1998 George Burch Memorial Lecture, Association of University Cardiologists
 2001 Plenary Lecture, Biophysical Society of Taiwan Seventh Annual Symposium on Recent Advances in Biophysics

Douglas G. Hill Memorial Lecturer, Duke University

Special Chair Professor, National Science Council, Republic of China

Barnett Lecture in Bioanalytical Chemistry, Northeastern University

2002 Harvard University Morrison Lecture

1992

1992

1994

1996

2004 McElvan Lecturer, University of Wisconsin, Madison on Analytical Chemistry

2005 Rachford Lecturer, Children's Hospital of Cincinnati

Baker Lecturer, Cornell University

2006 Honorary Faculty Member, Fourth Military Academy Medical University, Xi'an,

China

2008 Distinguished Lecturer, Center for Prostate Disease Research (DPDR), Rockville, MD

# Professional Affiliations and Service

1971-1975 NIH Study Section, BBCA

1972-1986 Editorial Board, Archives of Biochemistry and Biophysics

1972-1981 Editorial Board, Journal of Molecular Evolution 1972-1992 Editorial Board, Journal of Molecular Biology

1973-1986 Editorial Advisory Board, Biopolymers; Editorial Board, 1980-83

1973-1988 Editorial Board, Nucleic Acids Research

1974 Co-chairman, Biopolymers Gordon Conference

1974-1992 Harvey Society

1976-1988 Proposal Review Panel, Stanford Synchrotron Radiation Laboratory;

Chairman, 1980-88

1976-present Series Editor, Advanced Textbooks in Chemistry, Springer-Verlag, New York

1977-1981 CMBD Review Committee, NIGMS, NIH; Chairman, 1979-81

1978-1983 Editorial Board, Biochemistry

1978-1983 Board of Trustees, Cold Spring Harbor Laboratory

1978-present Biophysical Society; Council Member, 1978-81

1979-1981 Nominating Committee, American Chemical Society, Division of Biological

Chemistry

1982-1994

1983-1984

1980-1994 Society for Analytical Cytology

1981-1986 Editorial Board, Journal of Biological Chemistry

1982-present American Society of Biochemistry and Molecular Biology, formerly American

Society of Biological Chemists; Nominating Committee, 1982-83

Associate Editor, Annual Review of Biophysics and Biophysical Chemistry
National Research Council Committee on Causes and Effects of Changes in

Stratospheric Ozone

1983-1987 Consultant, Syntex Medical Diagnostics

1983-1987 Associate Editor, Journal of Molecular Evolution 1984-1985 Consultant, Lifecodes, Inc., formerly Actagen, Inc. 1984-1988 Editorial Board, Accounts of Chemical Research

1984-1988 Editorial Board, Accounts of Ch 1984-1988 Consultant, LKB-Produkter AB

1984-1989 Principal Investigator, Columbia University, Member of MacArthur

Foundation Consortium on the Biology of Parasitic Diseases

1984-1995 Advisory Council, Department of Molecular Biology, Princeton University
1984-1986 Scientific Advisory Board, American Cyanamid Company, Wayne, NI

1984-present Nomenclature Commission of the International Union of Biochemistry and

Molecular Biology

1985-1986 Office of Technology Assessment Advisory Panel on Determining

Mutation Frequencies in Human Beings

1985-1986 Consultant, Molecular Biophysics Technology, Inc.

1985-1989 National Research Council Committee on Research Opportunities in Biology

1985-1991 Board of Reviewing Editors, Science

1985-present Consultant, Genelabs, Inc., Redwood City, CA

1985-1994 U.S. National Committee of International Union of Pure and Applied

Biophysics; Vice Chairman, 1988-1990; Chairman, 1991-1994

1986 Chairman, Committee for External Review, Department of Genetics, Stanford

University

1986-1987 Department of Energy HERAC Subcommittee on the Human Genome
1986-1988 National Research Council Committee on the Human Genome

1986-1988 National Research Council Committee on the Human Genome 1986-1989 Council, National Institute of General Medical Sciences, NIH

1986-1989 Visiting Committee for Brookhaven National Laboratory Biology Department

1987-1989 Scientific Advisory Board, Hereditary Disease Foundation

1987-1994 Subject Area Editor, Genomics

1987-1994 Advisory Committee, Searle Scholars Program; Chairman, 1993-1994 1987-2000 Scientific and Technical Advisory Board, Prince Ventures Partner, III

1988-1991 Co-organizer, Three Cold Spring Harbor Laboratory Meetings on Genome

Mapping and Sequencing

1988-1996 Scientific Advisory Council, Roswell Park Memorial Institute

1988-2004 Biomedical Advisory Committee, Pittsburgh Supercomputing Center

1988-present Cell and Membrane Transport Commission, International Union of Pure and

Applied Biophysics

1988-1992 Chairman, Department of Energy Human Genome Coordinating Committee;

member, 1991-1994

1988-present Member, Executive Committee and Founding Council, International Human

Genome Organization [HUGO]; Vice President, 1990-present; Chairman, 1991-1995; Chair, HUGO Human Genome Mapping Committee [HGMC];

President, HUGO Americas, 1992-1997

1988-present Editorial Board, Current Opinion in Biotechnology

1988-1998 Consultant, Amersham-Pharmacia Biotechnology, formerly Pharmacia LKB

Biotechnology AB

1989-1990 Member, NAS/NRC Panel on Cooperation with the USSR on Structure of

the Eucaryotic Genome and Regulation of its Expression

1989-1991 Member, Executive Committee, Human Gene Mapping Workshops

1989-present American Society of Human Genetics

1989-1992 Co-chair, Human Genome I, II, III meetings

 1989-1994
 Scientific Advisory Committee, European Molecular Biology Laboratory

 1989-2004
 Advisory Committee, University of Pittsburgh Biotechnology Center

1990-1993 Advisory Committee, MacArthur Foundation Program in Parasite Biology 1990-1995 Member, Board of Scientific Counselors, National Center for Biotechnology

Information [NCBI], National Library of Medicine
1990-1998 Member, UNESCO Scientific Coordinating Committee on the Human

Genome Project

1991-1993 Member, Scientific Advisory Board, Ribogene, Inc.

1991-2002 Member, Advisory Board, Encyclopedia of Molecular Biology and Biotechnology 1992-1997 Member, Board of Directors, Chair, Scientific Advisory Board, ATGC/AT

Biochem, Inc.

CA

1992-2002 Member, Scientific Advisory Board, Aclara, Inc., formerly Soane Technologies,

Inc., Hayword, CA

1992-1994 Organizer, 1st through 3rd International Conference on Bioinformatics,

Supercomputing, and Complex Genome Analysis, Tallahassee, FL

1993-2000 Member, Board of Scientific Advisors, Mosaic Technologies, Inc., Boston, MA

1993-1998 Member, Plant Genome Science and Technology Coordinating Committee.

Department of Agriculture

1993-1994 Chair, European Bioinformatics Institute [EBI] Advisory Committee

1993-1998 Member, Scientific Advisory Committee, Incyte Pharmaceuticals, Inc., Palo Alto,

Charles R. Cantor 4 February 2010

1994-present Member, Advisory Board, Boston University Journal of Science Technology

and Law

1994-1998 Consultant, SEOUENOM, Inc., San Diego, CA

1994-2007 Co-chair, Biotechnology Advisory Committee, Fisher Scientific, Hampton, NH

1994-1998 Member, HERAC Genome Project Subcommittee

Consultant, Trichor, Boston, MA 1995-1998

1996-1997 Member, NRC Committee, "Bits of Power"

1996-2000 Consultant, AmberGen, Boston, MA

1996-2002 Member, Advisory Committee, ELBA Foundation, Italy

Member, DARPA Advisory Committee on Biological Warfare Defense 1997-2000

1997-1998 Treasurer, New England Complex Systems Institute

1996-2000 FASEB Consensus Committee on Federal Funding, representing the

Biophysical Society; Chair, DOE Subcommittee

1997-present Advisor, Techno Ventures Management, Munich

Consultant, Caliper, Inc., Palo Alto, CA 1996-2002

1997-2000 Member, The Protein Society

Ouest Scholar, Ouest Diagnostics, Inc., San Juan Capistrano, CA 1997-1999

Member, Defense Intelligence Agency Bio 2020 Red Team, Washington, D.C. 1998-present

1999-present Science Board, GENpathways, formerly CIStem, San Diego, CA

2000-2005 Consultant, Samsung SAIT, Korea

2000-present Board of Directors, Human BioMolecular Research Institute, San Diego.

CA 2000-2001 Editorial Advisory Board, Oxford University Press

2001-2009 Editorial Board, Proceedings of the National Academy of Sciences

2001-present Editorial Board, American Journal of PharmacoGenomics

Editorial Advisory Board, Genomics and Proteomics 2001-present

2001-2007 Member, Lawrence Livermore National Laboratories BBRP Board

2001-present Dean's Advisory Board, Division of Biology, University of California San

Diego

Industrial Advisory Board, Department of Chemistry and Biochemistry. 2001-present

University of California San Diego

Member, Board of Overseers, Brandeis University School of Science 2001-present

2001-2008 Scientific Advisor, Automated Cell, Pittsburgh, PA

2001-present Scientific Advisory Board, Cellicon, Boston, MA

2001-2003 Scientific Advisory Board, GeneFormatics, Inc., San Diego, CA

2001-2005 Scientific Advisory Board, Odyssey, Inc., San Ramon, CA Board of Directors, EXSAR, formerly know as Carta Proteomics, 2001-present

Monmouth Junction, NI

Editorial Team, Drug Discovery Today 2002-present

2002-2004 Board of Directors, SIGA Technologies, Inc., San Diego, CA

2002-2004 Board of Directors, Plexus Vaccine, San Diego, CA

2002-present Advisory Committee Member, Stockholm Strategic Research Foundation

2002-2008 Board of Directors, Molecular Sciences Institute, Berkeley, CA

Scientific Advisory Board, Rodi Pharmaceuticals, Del Mar, CA 2002-2007

Scientific Advisory Board, Buffalo Center of Excellence in Bioinformatics 2002-2007

Founder and Member, Board of Directors, 2002-03, SelectX 2002-present

Pharmaceuticals, Inc., Worcester, MA

2003-present Scientific Advisory Board, Strand Genomics, Bangalore, India

2003-present Member, Editorial Academy, International Journal of Oncology, Athens,

Greece

2003-present Member, National Advisory Board, Boston University Research Center for

Translational Genomics and Human Rights, Boston, MA

2004-present Scientific Advisory Board, GeneGo, St. Joseph, MI 2004-present Scientific Advisory Board, Modular Genetics, Woburn, MA

2004–present Scientific Advisory Board, NuAce Technologies, Ramat-Hasharon Israel

2004–present Scientific Advisory Board, NuAce Technologies, Ramat-Hasharon Israe 2004–present Scientific Advisory Board, Provid Research, Piscataway, NI

2004-present Scientific Advisory Board, StructureSpec, La Jolla, CA

2004-2006 Scientific Advisory Board, Joint Center for Structural Genomics (JCSG), La

Jolla, CA

2004-2007 Scientific Advisory Board, UppsalaBio-X, Uppsala, Sweden

2005-present Member, Board of Directors, Silicon Kinetics, San Diego, CA
2005-2006 Member, The National Academies Committee on Review of Departs

2005-2006 Member, The National Academies Committee on Review of Department of Energy's Genomics: GTL Program, Washington, DC

2006-present Member, National Academy of Sciences, Research at the Intersection of

the Physical and Life Sciences (RIPLS), Washington, DC

2006-present Member, Scientific Advisory Board, Cyntellect, Inc., San Diego, CA

2007-present Founder, CEO, Board of Directors, DiThera, Inc.

2007-present Founder, Chairman, Board of Directors, Retrotope, Inc., Los Altos, CA
2008-present Member, Scientific Advisory Board, Applied Vaccine Therapeutics (AVT),

White Plains, NY

2008-present Member, Moscow Rosnano Tech Advisory Board, Moscow, Russia

2009-present Chair, Scientific Advisory Board, Immunolite, Durham, NC

### Publications

- Over 450 Journal Articles
- Cantor, C. R., and Schimmel, P. R. Biophysical Chemistry. San Francisco: W.H. Freeman and Company, 1980. 3 Volumes.
- Cantor, C.R., and Smith C.L. Genomics: The Science and Technology of the Human Genome Project, Wiley, Interscience, 1999.

#### Patents

Cantor, C.R. and Schwartz, D.C.: Electrophoresis Using Alternating Transverse Electric Fields, Norway Euro Patent No. NO 0172156 C, granted 05/24/84

Cantor, C.R. and Schwartz, D.C.: Electrophoresis Using Alternating Transverse Electric Fields, Japanese Patent No. JP 3052907 B4, granted 05/24/84

 $Cantor, C.R.\ and\ Schwartz,\ D.C.:\ Electrophoresis\ Using\ Alternating\ Transverse\ Electric\ Fields,\ US\ Patent\ No.\ US\ 4,473,452,\ granted\ 09/25/84$ 

Cantor, C.R. and Schwartz, D.C.: Electrophoresis Using Alternating Transverse Electric Fields, Canadian Patent No. CA 1,207,275, granted 07/08/86

Cantor, C.R., Axel, R., and Argarana, C.: DNA Encoding Streptavidin, Streptavidin Produced Therefrom, Fused Polypeptides which Include Amino Acid Sequences Present in Streptavidin and Uses Thereof, European Patent No. EP 0258411, granted 08/27/87

Cantor, C.R., Axel, R., and Argarana, C.: DNA Encoding Streptavidin, Streptavidin Produced Therefrom, Fused Polypeptides which Include Amino Acid Sequences Present in Streptavidin and Uses Thereof, Japanese Patent No. JP 63802560, granted 08/27/87

Cantor, C.R., Axel, R., and Argarana, C.: DNA Encoding Streptavidin, Streptavidin Produced Therefrom, Fused Polypeptides which Include Amino Acid Sequences Present in Streptavidin and Uses Thereof, Australian Patent No. AU 7165287, granted 08/27/87

Saffran, W.A., Edelson, R.L., Gasparro, F.P., Welsh, J., and Cantor, C.R.: Biotinylated Psoralens, European Patent No. EP 0266212, granted 10/08/87

Saffran, W.A., Edelson, R.L., Gasparro, F.P., Welsh, J., and Cantor, C.R.: Biotinylated Psoralens, Australia Patent No. AU 7237287 A1. granted 10/08/87

Cantor, C.R. and Schwartz, D.C.: Gel Inserts Useful in Electrophoresis, US Patent No. US 4,695,548, granted 09/22/87

Collins, F., Weissman, S., and Cantor, C.R.: Coincidence Cloning Method and Library, Australia Patent No. AU 2318288 A1, granted 02/23/89

Cantor, C.R., Axel, R., and Argarana, C.: DNA Encoding Streptavidin, Streptavidin Produced Therefrom, Fused Polypeptides which Include Amino Acid Sequences Present in Streptavidin and Uses Thereof, US Patent No. US 4,839,293, granted 06/13/89

Cantor, C.R. and Schwartz, D.C.: Electrophoretic Methods Employing Gel Inserts, US Patent No. US 4,861,448, granted 08/29/89

Saffran, W.A., Edelson, R.L., Gasparro, F.P., Welsh, J.T., and Cantor, C.R.: Biotinylated Psoralens, US Patent No. US 4,868,311, granted 09/19/89

Van der Ploeg, L.H.T., Giannini, S.H., and Cantor, C.R.: Method for Detecting Animal-Infective Protozoa in vitro and a Method for Detecting Agents which Block the Differentiation Thereof, US Patent No. US 4,908,308, granted 03/13/90

Cantor, C.R., Köster, H., Smith, C.L., and Fu, D.J.: Solid Phase Sequencing of Biopolymers, European Patent No. EP 0830460, granted 11/06/92

Cantor, C.R. and Schwartz, D.C.: Electrophoresis Using Alternating Transverse Electric Fields, European Patent No. EP 0125310, granted 02/10/93

Cantor, C.R. and Schwartz, D.C.: Electrophoresis Using Alternating Transverse Electric Fields, Austria Euro Patent No. AT 0040752E, granted 02/10/93

Cantor, C.R. and Schwartz, D.C.: Electrophoresis Using Alternating Transverse Electric Fields, Australia Patent No. AU 565758, granted 02/10/93

Cantor, C.R. and Schwartz, D.C.: Electrophoresis Using Alternating Transverse Electric Fields, German Euro Patent No. DE 3379177 C0, granted 02/10/93

Cantor, C.R. and Schwartz, D.C.: Electrophoresis Using Alternating Transverse Electric Fields, Denmark Euro Patent No. DK 0169978 B1, granted 02/10/93

Cantor, C.R. and Schwartz, D.C.: Electrophoresis Using Alternating Transverse Electric Fields, Finland Euro Patent No. FI 0084518C, granted 02/10/93

Cantor, C.R., Chuck, R.S., and Tse, D.B.: Design and Synthesis of Bisecific DNA-antibody Conjugates, US Patent No. US 5,635,602, granted 08/13/93

Edwards, C.A., Cantor, C.R., and Andrews, B.M.: Screening Assay for the Detection of DNA-Binding Molecules, US Patent No. US 5,306,619, granted 04/26/94

Edwards, C.A., Cantor, C.R., Andrew, B.M., Turin, L.M., and Fry, K.E.: Sequence-Directed DNA-Binding Molecules Compositions and Methods, European Patent No. EP 0684999, granted 07/07/94

Edwards, C.A., Cantor, C.R., Andrews, B.M., Turin, L.M., and Fry, K.E.: Sequence-Directed DNA-Binding Molecules Compositions and Methods, Canadian Patent No. CA 2,152,501 A1, granted 07/07/94

Edwards, C.A., Cantor, C.R., Andrews, B.M., Turin, L.M., and Fry, K.E.: Sequence-Directed DNA-Binding Molecules Compositions and Methods, Australian Patent No. AU 685085, granted 07/07/94

Sano, T. and Cantor, C.R.: Recombinant Streptavidin-Protein Chimeras Useful for Conjugation of Molecules in the Immune System, US Patent No. US 5,328,985, granted 07/12/94

Cantor, C.R., Niemeyer, C.M., Smith, C.L., Sano, T., Hnatowich, D.J., and Rusckowski, M.: Self-Assembling Multimeric Nucleic Acid Constructs, European Patent No. EP 0744894, granted 08/03/95

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